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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/027,205	02/20/1998	CARL H. JUNE	36119-126	2825

7590 09/16/2005

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Naval Medical Research Center Office of Counsel
503 Robert Grant Avenue
Silver Spring, MD 20910-7500

EXAMINER

GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 09/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/027,205

Applicant(s)

JUNE ET AL.

Examiner

Phillip Gambel

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 September 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 96,97 and 99-107 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 96,97 and 99-107 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission, filed on 9/7/05, has been entered.

Applicant's amendment, filed 9/7/05, has been entered.

Claims 1-95 and 98 have been canceled.

Claims 96, 97, 101, 102 and 106 have been amended

Claims 96-97 and 99-107 are pending in the instant application.

2. Applicant's amended claims, filed 9/7/05, have obviated the previous rejections under 35 U.S.C. 112, first paragraph, enablement

3. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 96-97 and 99-107 are rejected under 35 U.S.C. § 103(a) as being unpatentable over June et al. (U.S. Patent No. 6,352,694) ('694) (of record) AND/OR June et al. (U.S. Patent No. 6,905,680) ('680) in view of Chang et al. (U.S. Patent No. 6,129,916) (of record) and newly added Kwon et al. (U.S. Patent No. 5,569,997) and Allaway et al. (US 2004/0086528 A1).

The teachings of June et al. (U.S. Patent No. 6,352,694) in view of and Chang et al. (U.S. Patent No. 6,129,916) are of record.

A more thorough review of applicant's arguments and the examiner's rebuttal of record with respect to these teachings can be found in the previous Office Actions.

June et al. in view of Chang et al. differ from the claims not measuring the level of CCR5 expression in T cells contacted with anti-CD3 and anti-CD28 antibodies.

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Newly added June et al. '680 provides for providing stimulating T cells from HIV-infected patients as well as for HIV-infected patients both in vitro and in vivo with anti-CD3 and anti-CD28 antibodies on the same solid surface, including beads (see entire document, including Summary of the Invention and Detailed Description of the Invention and Claims; also see Uses of the Methods of the Invention on columns 30-35). This reference further teaches the advantages of such procedures in providing for replenishing the immune response to said patients while providing HIV resistance (see Uses of the Methods of the Invention on columns 30-35 and Examples).

Although June et al. '680 teach the advantages of anti-CD3 and anti-CD28 antibody stimulation in the context of HIV-infected cells and treatment of HIV-infected patients, June et al. '680 does not teach the measuring CCR5 in the context of such treatment.

As pointed out previously, Kwon et al. teach that the ligation of T cells with anti-CD3 and anti-CD28 antibodies induce an HIV virus resistant state, which appears to be specific for macrophage-tropic HIV and appears to be the result of down-regulation of CCR5, the fusion cofactor (see entire document, particularly column 28, paragraph 1).

Again, Allaway et al. teach various methods to measure CCR5, including in assays measuring the effects of inhibiting fusion of HIV-1 to CD4⁺ T cells and infection of the cells (see entire document, including Summary of the Invention).

Given the teachings of the beneficial effects of contacting T cells with anti-CD3 and anti-CD28 antibodies to increase HIV resistance and that this beneficial effect was a result of down-regulation of CCR5 as taught by the prior art, one of ordinary skill in the art at the time the invention was made would have been motivated to monitor the expression of CCR5 expression to monitor the effect of combining anti-CD3 and anti-CD28 antibodies on T cell populations on HIV expression. In addition, the prior art provides for the co-immobilization of anti-CD3 and anti-CD28 on the same bead as a means of stimulating T cells. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

5. Applicant's arguments, filed 9/7/095, have been fully considered but have not been found convincing essentially for the reasons of record and those addressed herein.

Applicant's arguments concerning the Levine, Science 272: 1939-1942 (1996) have been rendered moot in that this Levine reference is no longer a part of the rejection.

Kwon et al. was added previously to provide for the ligation of T cells with anti-CD3 and anti-CD28 antibodies induce an HIV virus resistant state, which appears to be specific for macrophage-tropic HIV and appears to be the result of down-regulation of CCR5, the fusion cofactor (see entire document, particularly column 28, paragraph 1).

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While applicant asserts that the prior art including the June '694, Chang, Kwon, and Allaway prior art references do not teach the advantages of the bead versus other solid phase surfaces, applicant is invited to the teachings of June et al. '680, indicated above. Note that the claims of both June '694 and '680 do claim providing the anti-CD3 and anti-CD28 antibodies on the same solid surface, including a bead, to achieve the claimed methods.

In response to applicant's arguments against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 208 USPQ 871 (CCPA 1981). In re Merck & Co., Inc., 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to combine the teachings of the references to monitor the effectiveness of stimulating T cells with anti-CD3 and anti-CD28 antibodies to replenish the immune response of HIV-infected patients with the additional advantages of increasing HIV-resistance via the CCR5 pathway in part, as taught by the prior art above.

In this case the teachings of the prior art pertaining to the issues of immunodeficiencies in HIV-infected patients also indicated success in the relevant ability of stimulating T cells with anti-CD3 and anti-CD28 antibodies on the same solid surface, including beads, to restore immune responsiveness in said patients, including increasing the resistance of said treated T cells to HIV infection and persistence to combine the references to solve a well known problem in the art by one of ordinary skill in the art at the time the invention was made. The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983). See MPEP 2144.

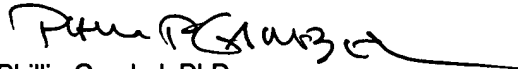
Applicant's arguments have not been found persuasive.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read "Phillip Gambel", with a long horizontal flourish extending to the right.

Phillip Gambel, PhD.

Primary Examiner

Technology Center 1600

September 14, 2005